Plasma Membrane II

I. Overview

A. Composition of Cellular and Extracellular Fluid

1. Na+ is higher outside the cell

2. K+ is higher inside the cell

3. Cl- is higher outside the cell

B. Lipid Bilayers

1. Maintain the differences in ECF and ICF concentration

2. Molecules will naturally diffuse down a gradient, if they can

C. External Signaling

1. Every external signal must directly or indirectly transverse the PM

2. Direct cell-to-cell communication from cytoplasm to cytoplasm

3. Extracellular molecules passing through the plasma membrane (via proteins)

4. Signal transduction – only the biomolecular signal crosses the membrane

D. Osmosis

1. Diffusion of water across of selectively permeable membrane

2. Water can also flow through channels called aquaporins

3. Water will flow from high H2O concentration 🡪 low H2O concentration

4. Osmotic pressure = pressure required to prevent net flow across membrane

II. Facilitated Diffusion

A. Carrier Mediated Facilitated Diffusion

1. Three main features differentiate from passive

a. Rate of facilitated is *much* higher than passive

b. Transport is specific

c. Transport occurs via a limited number of carrier proteins

2. Facilitated diffusion accelerates an already thermodynamically favored process

3. Carrier mediated facilitated diffusion is saturable

4. GLUT4 Transporter

a. Found in muscle and fat cells – associated with diabetes and obesity

b. Glc binds when [Glc] is high in the ECF

c. Glc binds to receptor, which undergoes a conformational change

i. Shifts glucose from outside to inside the cell

d. GLUT4 transporter is pre-synthesized and stored in vesicles

i. Insulin signals cell to transport GLUT4 to the surface

ii. Note than insulin never enters the cell

B. Ion Channel Mediated Diffusion

1. All cells maintain an electrochemical balance to survive

a. These gradients can be used as an energy source

2. Ion channels are a form of facilitated diffusion

3. Ion flow depends on both the electrical and chemical concentration gradients

4. Most ion channels are “gated”

a. Voltage-gated

b. Ligand-gated

c. Mechanically-gated

C. Voltage-Gated Channels

1. Structures of related α-helices combine to form a selective ion channel

a. Can either be multiple proteins or one long polypeptide chain

2. Part of the structure is made up of positively charged lysine AAs b. These AAs can sense changes in charge

3. Conformational change occurs at specific voltages 🡪 opens channel

a. Once open, inactivation domain physically occludes the channel

b. Rapid inactivation is key to function

c. Following depolarization, channel closes and occlusion is removed

D. Selectivity of Ion Channels

1. Most ion channels are highly selective

2. Note that all ions exist in a hydrated shell

3. At the selectivity filter of the channel, the pore size is too small for H2O to pass

a. The ion must shed its water shell

b. Ion-water interactions must be replace with ion-protein interactions

c. Must be energetically favorable for ion to pass through

d. AA structure favors interactions with specific ions, but not others

E. Speed of Ion Channels

1. Speed of transport is very fast

2. Electrostatic repulsions between ions in the channel force them through faster

a. Ions bind to part of the channel, then another ion pushes it through

i. Channels are specific, so all of the passing ions have like charges

F. Ligand Gated Ion Channels

1. nAChRs are found at the NMJ, allow passage of K+ and Na+

2. Acetylcholine (or nicotine) can bind to the receptor to allow ion influx

3. Normal conformation is impermeable to ions

a. Alanine residues block the opening of the channel

b. ACh binding causes a conformational shift that turns the alanines

c. Conformational change opens the channel as long as ACh is bound

4. Influx of cations causes membrane depolarization

G. Myasthenia Gravis

1. Part of a class of diseases called “channelopathies” – channel dysfunction

2. Hallmark is weakness is skeletal muscles, particularly the face

3. Body makes antibodies that either bind to and block or destroy nAChRs

a. Prevents binding of ACh and subsequent depolarization

b. Treatable with acetylcholinesterase inhibitors and immunosuppressants

III. Active Transport

A. Primary vs. Secondary

1. All active transport requires energy

2. If transporter protein itself hydrolyzes ATP

a. Primary Active Transport

3. If unfavorable flow of one molecule is couple to favorable flow of another

a. Secondary Active Transport

B. Three Families of Primary Active Transporters

1. P-class or P-type (ATP powered pumps)

2. ABC type (transporters)

3. F&V type (common in bacteria and plants, pumps H+)

C. P-Class ATP Powered Pumps

1. Hydrolyzes ATP to provide energy to pump against EC gradient

2. Requires Mg2+ cofactor

3. Na+/K+ ATPase

a. Found in all cells

b. Helps generate and maintain K+ and Na+ concentration gradients

c. High percentage of cytosolic ATP is used to power this pump

d. Cell exchanges 3 Na+ for 2 K+ with the use of 1 ATP

e. Bound phosphate – open to ECF, unbound phosphate – open to ICF

4. Cardiotonic Steroid Drugs

a. Old drug that could increase the strength of cardiac muscle contraction

b. Prevents dephosphorylation of protein, locking and deactivating it

c. Allows Na+ to build up, leading to an increase in Ca2+ (transporter action)

i. Ca mediated signals increase contraction strength of heart muscle

D. ABC Superfamily

1. ATP-Binding-Cassette

2. Transports ions and small molecules

3. ATP hydrolysis is coupled to solute movement

4. Requires 2 ATP to transport molecules

a. Phosphorylated state opens to ECF to release substrate to exterior

b. Dephosphorylation resets protein for another substrate to bind

5. MDR1

a. Involved in the failure of some drug therapies

b. Planar nonpolar molecules can diffuse through the PM

c. Uses ATP energy to export drugs from cytoplasm to the exterior

6. CFTR

a. Member of ABC superfamily

b. Cystic Fibrosis Transmembrane Regulator

c. Mutation is due to a deletion of 3 bp and loss of F508

d. Mutated protein is made, but it never makes it to the membrane

e. Normally involved in transported Cl- out of the cell

i. Accumulation of Cl- causes Na+ and H2O to enter the cell from ECF

ii. Results in thick, dehydrated mucus – defective respiratory cilia

E. Secondary Transporters

1. Symporter – transporter that moves two molecules in the same direction together

2. Antiporter – transporter that moves two molecules in opposite directions

3. Sodium/Glucose Symporter

a. Na is much more concentrated in the intestinal lumen than inside cells

b. Cells need to uptake Glc, so levels are higher intracellularly

c. Symporter can couple the movement of Glc with Na

i. Na down its gradient, Glc against gradient – total process favored